

CLAIMS

[00393] What is claimed is:

[00394] 1. A method of identifying a toxicologically relevant canine gene comprising the steps of:

[00395] (a) obtaining a gene expression profile of untreated canine cells;

[00396] (b) obtaining a gene expression profile of canine cells treated with an agent; and

[00397] (c) comparing the gene expression profile of untreated canine cell with the gene expression profile of the treated canine cells to obtain a gene expression profile indicative of a toxicological response.

[00398] 2. The method according to claim 1 wherein the canine cells are kidney cells.

[00399] 3. The method according to claim 2 wherein the kidney cells are MDCK cells.

[00400] 4. The method according to claim 1 wherein the canine cells are isolated from a biological sample.

[00401] 5. The method according to claim 1 wherein the gene expression profile is obtained by:

[00402] (a) providing canine cells;

[00403] (b) dividing said cells into two groups;

[00404] (c) using the first group of canine cells as a control group;

[00405] (d) exposing the second group of canine cells to an agent;

[00406] (e) isolating RNA from the first and second groups of canine cells;

[00407] (f) generating double stranded cDNA from said RNA;

[00408] (g) labeling said cDNA;

[00409] (h) resolving said cDNA on a gel; and

[00410] (i) comparing intensity of bands between the group of cells or tissue exposed to said agent and the group of cells or tissue not exposed to said agent.

[00411] 6. The method according to claim 5 wherein the gene expression profile is stored in a database.

[00412] 7. The method according to claim 1 wherein the gene expression profile is obtained by transcriptome profiling.

[00413] 8. The method according to claim 1 wherein said agent is an agent listed in Table 10.

[00414] 9. A method of isolating canine genes indicative of a toxicological response to an agent comprising the steps of:

[00415] (a) providing sequences of mammalian non-canine genes associated with toxicological responses;

[00416] (b) providing primers homologous to said genes; and

[00417] (c) using said primers to amplify canine genes from a canine cDNA library.

[00418] 10. The method according to claim 9 wherein the mammalian non-canine gene is a human gene.

[00419] 11. The method according to claim 9 wherein the mammalian non-canine gene is a rat gene.

[00420] 12. A method for determining a toxicological response to an agent comprising the steps of:

[00421] (a) exposing cells to an agent;

[00422] (b) obtaining a first gene expression profile from said cells;

- [00423] (c) comparing the first gene expression profile with a gene expression profile of toxicologically relevant canine genes; and
- [00424] (d) determining if the first gene expression profile is indicative of a toxicological response.

[00425] 13. The method according to claim 12 wherein at least one gene expression profile of a toxicologically relevant canine gene is stored in a database.

[00426] 14. The method according to claim 12 wherein said toxicological response is selected from the group consisting of a cellular response, pathological change, and histological change.

[00427] 15. A method for determining a toxicological response in an organ to an agent comprising the steps (a) - (c) according to claim 12 and further comprising an additional step of determining if the first gene expression profile is indicative of a toxicological response in an organ.

[00428] 16. The method according to claim 15 wherein said toxicological response is a change in physiological function of the organ.

[00429] 17. A method for screening an agent for a potential toxicological response comprising the steps of:

- (a) exposing cells to an agent;
- (b) obtaining a first gene expression profile from said cells;
- (c) comparing the first gene expression profile with a gene expression profile of toxicologically relevant canine genes to determine if the first gene expression profile is indicative of a toxicological response in genes associated with toxic responses.

[00430]

[00431]

[00432]

[00433] 18. The method according to claim 17 wherein at least one gene expression profile of a toxicologically relevant canine gene is stored in a database.

[00434] 19. The method according to claim 17 wherein said agent is a drug.

[00435] 20. The method according to claim 17 wherein said agent is a pharmaceutical composition.

[00436] 21. A method for generating a canine array comprising isolating at least ten canine genes which are indicative of a toxicological response and attaching said genes to a substrate.

[00437] 22. The method according to claim 21 wherein said substrate is a solid substrate.

[00438] 23. The method according to claim 22 wherein said solid substrate comprises glass.

[00439] 24. An array comprising of at least ten canine toxicological response genes or a portion thereof immobilized on a substrate.

[00440] 25. The array according to claim 24 wherein said substrate is a solid substrate.

[00441] 26. The array according to claim 25 wherein said solid substrate comprises glass.

[00442] 27. The array according to claim 24 wherein said genes are attached to said substrate by covalent linkage.

[00443] 28. The array according to claim 24 wherein said genes or portions thereof are capable of hybridization to expressed nucleic acids derived from a cell and are capable of indicating a toxic response of the cell to said agent.

[00444] 29. The array according to claim 24 wherein said genes have a gene expression indicative of toxicological response to an agent listed in Table 10.

[00445] 30. The array according to claim 24 comprising at least 10 canine toxicological genes or a portion thereof.

[00446] 31. The array according to claim 24 comprising at least 25 canine toxicological genes or a portion thereof.

[00447] 32. The array according to claim 24 comprising at least 50 canine toxicological genes or a portion thereof.

[00448] 33. The array according to claim 24 comprising at least 100 canine toxicological genes or a portion thereof.

[00449] 34. The array according to claim 24 comprising at least 250 canine toxicological genes or a portion thereof.

[00450] 35. The array according to claim 24 comprising at least 500 canine toxicological genes or a portion thereof.

[00451] 36. The array according to claim 24 comprising at least 750 canine toxicological genes or a portion thereof.

[00452] 37. The array according to claim 24 comprising at least 1000 canine toxicological genes or a portion thereof.

[00453] 38. An array comprising at least 10 genes of Table 8.

[00454] 39. An array comprising at least 10 genes of Table 9.

[00455] 40. A method for obtaining a gene expression profile comprising exposing a population of cells to an agent, obtaining cDNA from said population of cells, labeling said cDNA, and contacting said cDNA with the array according to claim 20.